Case Report

Multiple angiomyolipomas mimicking metastases of concurrent clear cell renal cell carcinoma

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Abbreviations & Acronyms
AML = angiomyolipoma
ccRCC = clear cell renal cell carcinoma
CRP = C-reactive protein
CT = computed tomography
HMB = human melanoma black
LDH = lactate dehydrogenase
LN = lymph node
TSC = tuberous sclerosis complex
αSMA = α-smooth muscle actin

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Introduction: Concurrence of clear cell renal cell carcinoma and angiomyolipoma is quite rare. We report a case of large localized clear cell renal cell carcinoma with concurrent multiple angiomyolipomas mimicking lymph node metastases.

Case presentation: A 60-year-old woman presented with general malaise, weight loss, and intermittent fever. Computed tomography scan demonstrated an 8-cm mass in the left kidney, enlarged para-aortic lymph nodes, and small renal nodules adjacent to the main tumor. She was diagnosed preoperatively as having clear cell renal cell carcinoma (cT3a) with multiple para-aortic lymph node metastases, and underwent laparoscopic radical nephrectomy and dissection of the para-aortic lymph nodes. Pathologically, the main tumor was diagnosed as clear cell renal cell carcinoma. By contrast, both the para-aortic lymph nodes and nodules were diagnosed as lipid-poor angiomyolipomas.

Conclusion: With the expanding first-line use of molecular targeted therapy for metastatic renal cell carcinoma, nephrectomy may be avoided by overdiagnosis. Upfront nephrectomy can avoid overdiagnosis and undertreatment of nonmetastatic renal cell carcinoma.

Key words: clear cell renal cell carcinoma, kidney cancer, lipid-poor angiomyolipoma, multiple angiomyolipomas.

Keynote message

Concurrence of ccRCC and AML is quite rare. With the expanding first-line use of molecular targeted therapy for metastatic RCC, nephrectomy may be avoided by overdiagnosis. Upfront nephrectomy can avoid overdiagnosis and undertreatment of nonmetastatic RCC.

Introduction

It is well known that AML is the most common benign tumor of the kidney whereas ccRCC is the most common malignant one.[1] Concurrence of RCC and AML is quite rare,[2–5] and even the latest imaging modalities still have limited efficacy for distinguishing lipid-poor AML from ccRCC.[6–8] In general, the probability of synchronous metastasis of RCC increases with tumor size, and the median diameter of RCC with synchronous metastasis is 8.0 cm.[9] Therefore, precise preoperative diagnosis of concurrent large RCC and small AMLs is considered to be difficult. Herein, we report a case of large localized ccRCC with concurrent multiple AMLs mimicking LN metastases of ccRCC.

Case presentation

A 60-year-old woman was referred to our hospital for assessment of general malaise, anorexia, weight loss, and intermittent fever. She had no medical history of TSC. Contrast-enhanced CT demonstrated a well-enhanced renal mass 8 cm in diameter with central necrosis at the lower pole of the left kidney (Fig. 1a). Enlarged well-enhanced para-aortic LNs and small nodules

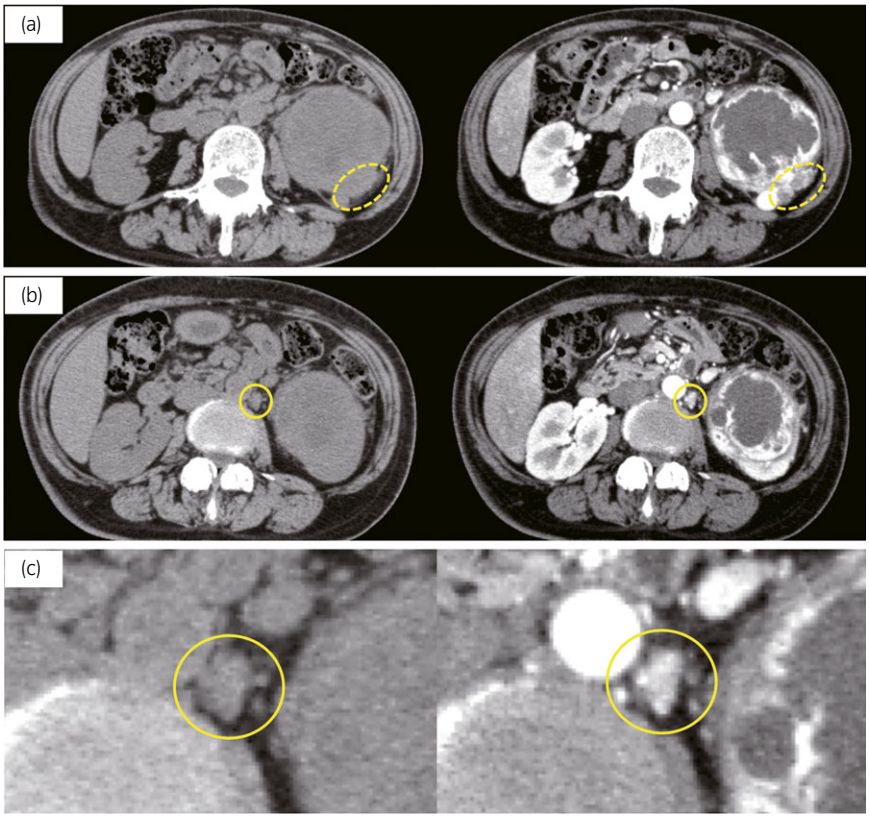

Fig. 1 Noncontrast (left side) and contrast-enhanced (right side) CT shows a well-enhanced tumor 8 cm in diameter with central necrosis at the lower pole of the left kidney. Dashed yellow circles indicate well-enhanced small nodules adjacent to the tumor (a). Well-enhanced para-aortic LNs are also indicated by yellow circles (b). Within the LNs, no findings of low-density area which indicates a fat component.

adjacent to the main renal tumor were also evident (Fig. 1a, b). Within the enlarged LNs, no low-density area indicating a fat component was detected by CT scan (Fig. 1c). Therefore, the patient was diagnosed preoperatively as having ccRCC (cT3a) with multiple para-aortic LN metastases. Laboratory data indicated anemia (hemoglobin 9.3 g/dL), hypercalcemia (corrected calcium 10.65 mg/dL), thrombocytosis (platelets 448 000/μL), an elevated CRP level (15.68 mg/dL), and a slightly low LDH level (111 U/L). The patient was classified as poor risk on the basis of the International Metastatic Renal Cell Carcinoma Database Consortium criteria.[10] We considered the multiple LN metastases to be confined to the para-aortic region and resectable. Therefore, we performed laparoscopic radical nephrectomy and para-aortic LN dissection. Pathologically, the cells in the main renal tumor showed clear cytoplasm with atypical nuclei, and the diagnosis was ccRCC (pT2a) localized to the left kidney (Fig. 2a–c). In contrast, the dissected para-aortic LNs (n = 13/32) contained blood vessels, muscle cells, and a small amount of adipose tissue (Fig. 2d,e). The small nodules adjacent to the main tumor also showed the same features as the LNs (Fig. 2f,g). Immunohistochemistry showed that the LNs and pararenal nodules were positively stained for αSMA and partially stained for HMB-45 (Fig. 2h, i). On this basis, they were diagnosed as AMLs of the para-aortic LNs and kidney. At 36 months after surgery, a small lung metastasis of ccRCC arose and was resected.

Discussion

There are several hypotheses to explain the co-occurrence of AML and RCC: (i) both arise from the same stem cells, as they exhibit similar expression of epithelial markers;[3] (ii) AML and RCC can be coincidentally present at the same location;[11] and (iii) RCC develops from AML, as it arises within preexisting AML during long-term follow-up.[4] Currently, there is still no consensus regarding these theories. In the present case, the main large RCC was located adjacent to small AMLs. However, morphological continuity among them was ruled out by pathological examination. Therefore, we were at least able to conclude that the RCC had not arisen from within preexisting AMLs in this case. Multiple AMLs were seen in the left kidney and para-aortic LNs in the present case. However, previous reports have concluded that this situation does not indicate multiple metastases of AML from a single origin, but rather multicentric occurrence of AML. For this reason, the prognosis was favorable after surgical resection.[12] Similarly, local recurrence of AML after complete surgical resection was also assumed to represent metachronous multicentric occurrence.[13] Although epithelioid AML with multiple metastatic LNs has been reported,[14] the present case did not exhibit characteristics of epithelioid AML such as sheets of epithelioid cells with atypical nuclei. Therefore, the AMLs in the present case were considered as multicentric occurrences.

AML frequently occurs in patients with TSC.[15] By contrast, a meta-analysis has demonstrated no increased risk of RCC in patients with TSC.[16] Jimenez *et al.* reported that one-third of cases of concurrent AML and RCC arose in patients with TSC and that two-thirds of them were sporadic.[2] The present patient did not meet the diagnostic criteria for TSC,[15] and therefore, this was considered to be a sporadic case.

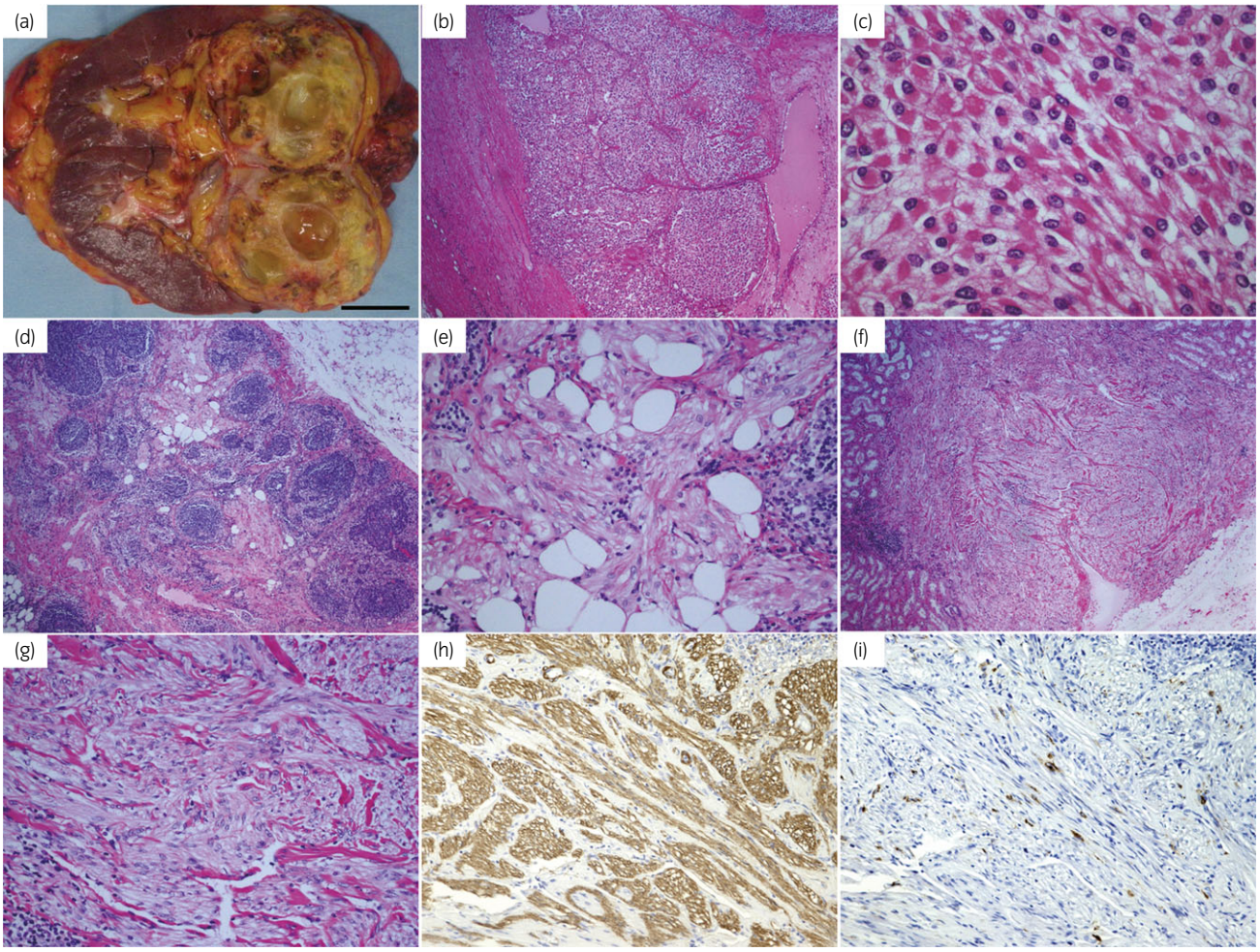

Fig. 2 Histopathological findings. (a) A yellowish tumor 8 cm in diameter is present at the lower pole of the left kidney. (b,c) Cells in the tumor in the left kidney show clear cytoplasm with atypical nuclei, typical of ccRCC (hematoxylin-eosin stain, ×40 and ×400). (d,e) Adipose tissue, blood vessels and muscle cells are evident in the dissected para-aortic LNs (hematoxylin-eosin stain, ×40 and ×200). (f,g) Nodules adjacent to the renal tumor also show the same features as the para-aortic LNs (hematoxylin-eosin stain, ×40 and ×200). (h,i) Immunohistochemistry shows that the LNs and the pararenal nodules are positively stained for αSMA (×200) and partially positive for HMB-45 (×200), leading to a diagnosis of AML of the para-aortic LNs and kidney (scale bar, 3 cm).

In the era of cytokine therapy, cytoreductive nephrectomy has been basically performed as far as practicable for metastatic ccRCC.[17] The development of molecular targeted therapy has meant that nephrectomy is being performed less often, especially for patients in poor general condition or with a large total volume of metastatic tumors.[18] The current National Comprehensive Cancer Network[19] and European Association of Urology[20] guidelines recommend molecular targeted therapy or immune checkpoint inhibitors as the first-line treatment, irrespective of whether cytoreductive nephrectomy is performed.

CT is unable to detect fat components in approximately 4.5% of AMLs that are defined as lipid-poor AMLs.[6] The sensitivity of CT for diagnosis of AML is reported to be only 46.0%, and most of the missed cases are lipid-poor AMLs.[7] A homogeneous enhancement pattern and high unenhanced attenuation on CT are reported to be sensitive and specific for lipid-poor AML.[6] Moreover, texture analysis has been shown to improve the diagnostic accuracy for lipid-poor AML.[8] However, no definitive method for correct preoperative diagnosis of lipid-poor AML has yet been established. We preoperatively diagnosed the present patient as having ccRCC (cT3a) and multiple para-aortic LN metastases. If concurrent AMLs are located at distant sites such as the lung or mediastinum, they might be preoperatively diagnosed as distant metastases of RCC. In this scenario, it may be necessary to avoid nephrectomy depending on the condition of the patient, and the opportunity for eradication might be lost with the expanding use of molecular targeted therapy as an initial treatment for metastatic RCC. To avoid this situation, accurate tumor characterization is essential. Moreover, upfront nephrectomy can avoid overdiagnosis and undertreatment of nonmetastatic RCC. Further improvement of diagnostic imaging technologies and development of new specific biomarkers for RCC and AML may have key roles to play in more precise preoperative diagnosis in the future.

Conflict of interest

The authors declare no conflict of interest.

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